Atrazine/Syngenta PC Code 080803 I

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: 5 Sept 2007

Subject: Atrazine: Magnitude of the Residues in or on Sugarcane, Including Processed Sugarcane Commodities. Final Report. MRID 47089002. DP# 341877, 338720

From: Dave Soderberg, Chemist
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To: Tracy Perry, Risk Manager Reviewer
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This study was submitted in response to a data call in listed in the Atrazine RED (DP # 272006. "Atrazine. HED Product and Residue Chemistry Chapters," 4/16/2002, by C. Eiden and D. Soderberg) to address the a need to reassess tolerances for the processed products of sugarcane.

Field trials were carried out at sites in FL and LA during 2003. A 4 lbs ai/gallon liquid formulation of atrazine (AAtrex 4L) was applied to sugarcane in a total of 10 lbs ai/A/season (1x) This total application consisted of four individual applications: one pre-emergent of 4 lbs ai/A; one at emergence of 2 lbs ai/A; one postemergence of 2 lbs ai/A (at 150 days PHI); and one postemergence of 2 lbs ai/A (at 120 days PHI). For each field trial there was also a 3X treatment with a total 30 lbs ai/A (12 +6+6+6 lbs ai/A), and a 5x treatment at 50 lbs ai/A (20+10+10+10). All treatments were made using between 20 -- 100 gallons/A.

Samples of the sugarcane were processed, "following commercial procedures," into molasses and refined sugar. This process was only cryptically described in this study with a flow diagram, but HED accepts that diagram as adequate for the purpose of this study. Samples were then analyzed using methods for residues of atrazine and its chloro-metabolites (G30033, G28279 and 28273) that was concurrently validated on raw sugarcane (but not on sugar or molasses). The samples were also analyzed for two of the hydroxy-metabolites of atrazine that were concurrently validated to an LOQ of 0.05 ppm

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A.B. RAC

in sugarcane. HED concurs that recoveries of the chloro-metabolites from sugarcane RAC are adequate to support use of the method on molasses and and refined sugar as well.

Detailed results of the study are described in the attached der Residues of atrazine in sugarcane treated at 5X were significant, and did not concentrate in either the sugar or molasses. Residues of other metabolites at 5X were not detectable in the RAC and did not discernably concentrate in either processed product, and, in any case, were minor components of the residue in comparison to the concentration of the parent.

Because residues do not concentrate in sugar or in molasses, there is no need for a revised dietary exposure assessment to address the results of this study, and separate tolerances for sugar and molasses are not required.

Attachments
47089002.der

RDI: David Soderberg (5 Spet 2007); William Donovan (5 Sept 2007); Cathy Eiden (5 sept 2007).
DP Number(s): 341877, 338720

Primary Evaluator — David Soderberg, Chemist, RRB3, HED — Date: 30 Aug 2007

Approved by — William Donovan, Senior Chemist, RRB3, HED — Date: 30 Aug 2007

STUDY REPORT:

MRID 47089002. Vincent, T. P. (2007) Atrazine: Magnitude of the Residue in or on Sugarcane Including Processed Sugarcane Commodities: Lab Project Number: T000146-03. Unpublished study prepared by Syngenta Corporation. 267 pages. DP# 341877, 338720

EXECUTIVE SUMMARY:

In each of two field trials conducted in FL and LA during 2003 a 4 lbs ai/gallon liquid formulation of atrazine (AAtrex 4L) was applied to sugarcane in a total of 10 lbs ai/A/season (1x). This total seasonal application consisted of four individual applications: one pre-emergent of 4 lbs ai/A; one at emergence of 2 lbs ai/A; one postemergence of 2 lbs ai/A (at 150 days PHI); and one postemergence of 2 lbs ai/A (at 120 days PHI). In addition to the 1x treatment, at each of these field trial sites there was also a 3X treatment with a total 30 lbs ai/A (12 +6+6+6 lbs ai/A), and a 5x treatment at 50 lbs ai/A (20+10+10+10). All treatments were made using between 20 – 100 gallons/A.

At 120 days after the last treatment (DAT), a control sample and a treated sample of raw sugarcane were harvested from 12 sites through out each plot by cutting 20 cm lengths, with leaves attached, from the top, middle and bottom of the sugarcane stems. These 20 cm stem lengths were then apportioned into samples as one third each, of top, middle and bottom pieces, so that the entire cane is appropriately represented. Inedible portions were removed and soil was brushed off, but the stems were not washed. The sugarcane samples were processed into molasses and sugar following "commercial practice" (see Figure B.1.) The RAC and its processed commodities were and analyzed for atrazine and its chloro-metabolites: G28279, G30033 and G28273, and separately for the hydroxyl-metabolites G34048 and GS17794 (see table A.3.).

Samples of sugarcane were stored and shipped frozen to Texas A & M University for processing. After processing into sugar and molasses, samples of RACs and processed products were frozen and shipped frozen to Syngenta in Greensboro, NC for analysis. From sampling to extraction samples were stored frozen for a maximum of 8.4 months for samples to be analyzed for atrazine, G28279, G30033 and G28273. Samples were stored frozen for up to 34.7 months prior to analysis for G34048 and GS17794. No concurrent stability study appears to have been performed, but storage stability of the chloro-residues in corn and apples have been shown to be stable for up to 25 months, except for G28273, which started to decline after 12 months. Separately, G24048 and GS17794 were shown to be stable for up to 36 months in corn fodder,

grain and in sorghum forage. This data should adequately support the stability of these analytes in sugarcane during frozen storage.

Residues of atrazine and its chloro-metabolites in/on sugarcane commodities were determined using Syngenta method 484. Concurrent recoveries from raw sugarcane show this to be an adequate GC/NPD method with an LOQ of 0.05 ppm. Although concurrent recoveries were not performed for sugar or molasses, HED agrees that recoveries from these two commodities are likely to be acceptable if recoveries from sugarcane are acceptable. In this method, a separate protocol is used to determine G28273. For determination of hydroxy-metabolites, method GRM014.01A was used. This hydroxy-method is a modification of Syngenta's Method AG-596 with an LOQ of 0.01 ppm, and used detection by LC/MS/MS. For determination of GS27794, the molecular ion (170.1) is monitored and a daughter ion (128.1) is determined by MS/MS. For G340048, MS/MS follows the parent molecular ion 198.2 and daughter ion 156.2. This method is also validated by concurrent recoveries with an LOD of 0.01 ppm.

Following the highest treatments at 5x, chloro-residues were <1.65 ppm in the RAC. Residues were <0.01 ppm for each of the hydroxyl-metabolites on the sugarcane and were 0.03 ppm in molasses and <0.01 ppm in refined sugar.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the sugarcane processing study is scientifically acceptable except that the processing to sugar and to molasses is not well described. HED will accept the cursory description provided for this particular application. The acceptability of this study for regulatory purposes is addressed in the accompanying cover memo (DP Number 338720).

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Atrazine is a triazine herbicide used to control annual broadleaf weeds in corn, guava, macadamia nuts, sorghum, sugarcane, range grasses and wheat. Atrazine is currently registered to Syngenta as FlC and WDG (dry flowable DF) formulations. It is applied either as a broadcast or as a banded pre-emergence, preplant or early postemergence application using either ground or aerial equipment. Permanent tolerances are established for residues of atrazine in/on numerous plant commodities at levels ranging from 0.05 ppm in/on guava to 15 ppm in/on field corn. [40 CFR §180.220(a)(1)]. Tolerances have been established under 40 CFR 180.220(a)(1) for residues in/on sugarcane and sugarcane forage and fodder at 0.25 ppm, expressed in terms of Atrazine, parent only.

The current sugarcane processing study was submitted by Syngenta in response to a DCI in the atrazine RED ((DP # 272006). The processing steps in this study are not well described, but HED will accept these processing studies as adequate to address the particular purpose of processing of atrazine treated sugarcane into its primary commercial commodities: molasses and sugar.

The nomenclature and physicochemical properties of atrazine are presented below in Tables A.1 and A.2.

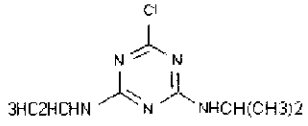
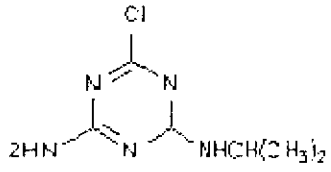
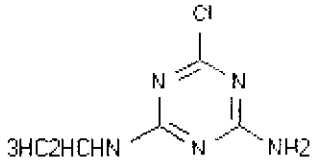
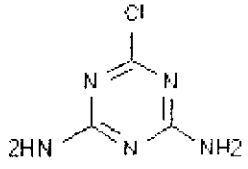
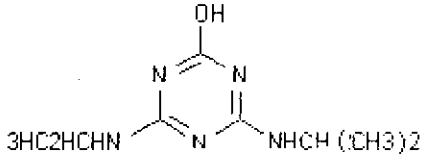
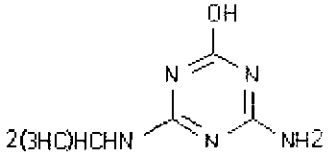
TABLE A.1. Atrazine Nomenclature.	
Compound	
Common name	Atrazine
Company experimental name	G-30027
IUPAC name	6-Chloro-N-ethyl-N-isopropyl-[1,3,5]triazine-2,4-diamine
CAS name	1,3,5-Triazine-2,4-diamine, 6-chloro-N-ethyl-N'-(1-methylethyl)-
CAS registry number	1912-24-9
End-use product (EP)	AAtrex® 4L

TABLE A.2 Physicochemical Properties of Atrazine.		
Parameter	Value	References
Melting point/range	176.0° C	MRID 00142160, 00164822, 43337901, 230302, Ciba Analytical Test #AG-87, Syngenta Study #1744-02
pH	7.0 at 25° C	
Relative Density (20°C)	0.37 g/cm^3	
Water solubility (20°C)	0.033 g/L	
Solvent solubility (g/100 mL at 20°C)	Solvent grams/100 mL solvent Acetone 3.2 Octanol 0.92 Ethanol 1.11 Toluene 0.42 Hexane 0.01	
Vapor pressure	2.89 x 10^{-7} mm Hg	
Dissociation constant, pK_a	PKa = 1.60 @ 20° C	
Octanol/water partition coefficient, Log(K_{OW})	481 (log P_{ow} = 2.68) at 25° C	
UV/visible absorption spectrum	Neutral 39,661 l/mol*cm@222.5 nm 3,274 l/mol*cm@263.5 nm Acidic 33,363 l/mol*cm@222.5 nm Basic 37,921 l/mol*cm@222.5 nm 4,609 l/mol*cm@263.5 nm	

Table A-3. Atrazine metabolites

Metabolite	Structure
G30033	
G28279	
GG28273	
G340048	
GS27794	

B. EXPERIMENTAL DESIGN

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics				Meteorological Data	
	Type	%OM[1]	pH	CEC[2] (meq/g)	Monthly Rainfall (inches)	Overall temp. (°F)
Washington, LA 2003	Clay	1.9	6.8	23.6	1.93 – 7.33	63.8- 83.6
Vero Beach, FL, 2003	Peat/Muck	61.4	7.3	68.6	1.69-9.71	62.8 – 83.2

1. OM = organic matter
2. CEC = Cation Exchange Capacity

B.1. Application and Crop Information

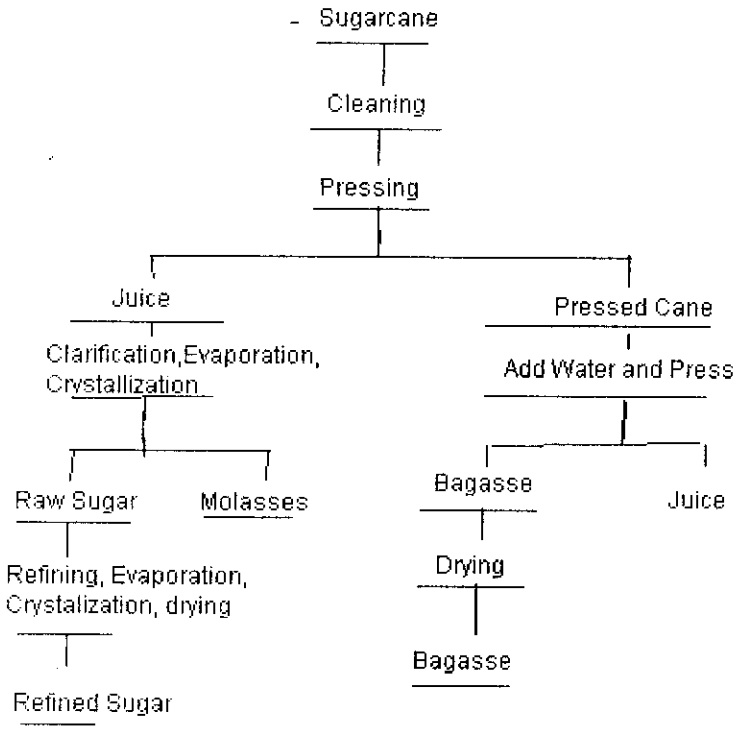
Table B.1. Study Use Pattern

Location (County, State; Year) Trial ID	End-use Products	Application Information				Tank Mix/ Adjuvants	Harvest Procedures
		Method; Timing	Single Rate (lb ai/A)	RTI [1] (days)	Total Rate (lb ai/A)		
Washington, LA/2003	AAtrex 4L	Pre-emergent, at emergence, 150 days PHI, 120 days PHI	none	none	No application	none	Hand cut, not stripped, cleaned or washed
		Pre-emergent, at emergence, 150 days PHI, 120 days PHI	4,2,2,2	18-25, 57-71, 29-30	10 lbs ai/A	none	Hand cut, not stripped, cleaned or washed
		Pre-emergent, at emergence, 150 days PHI, 120 days PHI	12,6,6,6	18-25, 57-71, 29-30	30 lbs ai/A	none	Hand cut, not stripped, cleaned or washed
		Pre-emergent, at emergence, 150 days PHI, 120 days PHI	20, 10, 10, 10	18-25, 57-71, 29-30	50 lbs ai/A	none	Hand cut, not stripped, cleaned or washed
Vero Beach, FL/2003	AAtrex 4L	Pre-emergent, at emergence, 150 days PHI, 120 days PHI	none	None	No application	none	Hand cut, not stripped, cleaned or washed
		Pre-emergent, at emergence, 150 days PHI, 120 days PHI	4,2,2,2	18-25, 57-71, 29-30	10 lbs ai/A	none	Hand cut, not stripped, cleaned or washed
		Pre-emergent, at emergence, 150 days PHI, 120 days PHI	12,6,6,6	18-25, 57-71, 29-30	30 lbs ai/A	none	Hand cut, not stripped, cleaned or washed
		Pre-emergent, at emergence, 150 days PHI, 120 days PHI	20, 10, 10, 10	18-25, 57-71, 29-30	50 lbs ai/A	none	Hand cut, not stripped, cleaned or washed

B.2. Sample Handling and Processing Procedures

Sugarcane samples were frozen within the day of harvest and stored/shipped frozen until processed to the processing facility, then were held frozen until analysis. Sugarcane samples were processed according to simulated commercial procedures into molasses and sugar. (Figure B.1) This flowchart was the only description of prodessing that was provided, however HED will accept it as adequate because sugar processing is well standardized.

FIGURE B.1. Processing Flowchart for Sugarcane



B.3. Analytical Methodology

Residues of atrazine and its chloro-metabolites in/on sugarcane commodities were determined using method 484, a Syngenta GC/NPD method with an LOQ of 0.05 ppm that was adequately validated by concurrent recoveries for use on sugarcane. This procedure provides separate determination of atrazine, G30033, and G28279 as one fraction and G28273 as another fraction. For the first fraction the sample is extracted by reflux with 80:20 methanol:water; then the extract is concentrated and applied to an Extrelut SPE column, where it was allowed to absorb for 20 minutes. The column is eluted with 250 mL of 15:85 ethyylacetate:hexane, and the eluant is concentrated to dryness. The sample is taken up in 5 mL of toluene, and 2 mL of hexane added, then it was loaded onto an Alumina B Sep Pak, which is then eluted with 30:70

methanol:acetonitrile. The eluate is evaporated to dryness, brought up in 95:5 ethyl acetate:methanol and analyzed by GC with a DB wax column and using an NPD.

Residues of G28273 were extracted as above, loaded onto an Extrelut column and eluted with 50:50 ehtyl acetate:hexane, dried, taken up in 8 mL of ethyl acetate and 8 mL of toluene was added. This solution was loaded onto a Fluorisil Sep-Pak, which was then washed with 5 mL dichloromethane, and the G28273 was eluted with 80:20 ethylacetate:methanol. This solution was dried, reconstituted in 95:5 ethylacetate:methanol and G28273 was determined by GC, DB wax column, with an NPD.

For determination of hydroxyl-metabolites, method GRM014.01A was used. This method is a modification of AG-596 with an LOQ of 0.01 ppm, and used detection by LC/MS/MS. In this method the sample is refluxed for an hour in 25:75 methanol:water. The extract is cooled, dilute HCl is added, and the extract is washed twice with 80:20 methylene chloride:hexane. 100 mL of 0.5 HCl is added to the aqueous phase and the sample is refluxed for 1.5 hours. After cooling a 10 mL aliquot is taken, ammonium acetate and 0.25 mL of concentrated ammonium hydroxide are added, and the resulting solution is diluted with 70:30 ammonium acetate(aq):methanol. The hydroxyl-metabolites are determined by HPLC on an Inertsil C-8 column 2%ammonium acetate/50:50 methanol:acetonitrile. For determination of GS27794, the molecular ion 170.1 is monitored and the daughter ion 128.1 is determined by ms/ms. For G340048, MS/MS follows the parent molecular ion 198.2 and daughter ion 156.2.

C. RESULTS AND DISCUSSION

The method was adequately validated for analysis of the RAC using concurrent recoveries. No concurrent recoveries of the chloro-residues were performed in molasses and sugar. However, since the recoveries are adequate for the RAC, recoveries of the chloro-metabolites are also expected to be adequate for these two processed products. Note, however, that this decision is specific to these products. Ordinarily, recoveries are needed for processed products, as well as for the RACs. For the RAC, concurrent recoveries of the chloro-metabolites ranged from 77-91% (Table C.1). Recoveries of the hydroxy-metabolites were performed in both the RAC and the molasses and sugar. Recoveries of G34048 from the RAC averaged 88%, and averaged 76% and 88% in the molasses and sugar, respectively. Recoveries for GS17794 averaged 94% in the RAC and 113% and 76% from molasses and sugar, respectively. The highest relative standard deviation (RSD) for the hydroxy-metabolite recoveries was 15.1%.

Apparent residues of atrazine and its metabolites were <LOQ in all control samples except for G30033 in molasses, which was at 0.06 ppm (just above the LOQ). Treated samples of molasses were at 0.08 ppm for G30033 molasses, but because the control was also slightly high, it is assumed that, for practical purposes, all G30033 residues in molasses should properly be considered to be non-detectable (ND), i.e. <0.05 ppm. Adequate samples calculations were provided along with example chromatograms. The method LOQ for the chloro-metabolites is 0.05 ppm and the method LOQ for the hydroxyl-metabolites is 0.01 ppm.

Concurrent storage stability determinations were not performed, however, storage stability data are available from other commodities indicating that atrazine and its metabolites are expected to be stable for the storage periods used in this study (see table C.2.).

Following application of atrazine at 50 lbs ai/A (5x rate), the residues of atrazine in/on sugarcane RAC are 1.5 ppm. Residues of other atrazine metabolites are undetectable on the RAC. Residues of atrazine and its metabolites are all undetectable in molasses and sugar. This result indicates that atrazine is not concentrated in either processed product. A processing reduction factor of 0.12 may be applied to molasses and sugar.

The maximum theoretical concentration factor for sugarcane to sugar is 11.8. There is no maximum concentration factor for sugarcane molasses.

TABLE C.1. Summary of Concurrent Recoveries of Atrazine from Sugarcane and the Sugarcane Processed Products, Molasses and Sugar.

Matrix	Metabolite	All Spike levels (ppm)1	Sample size (n)	Recoveries (%)	Mean ± std dev (RSD) (%)
Sugarcane RAC	Atrazine	0.01, 0.05, 0.1, 0.2, 2.0	12	87, 95, 74, 84, 107, 82, 85, 102, 84, 94, 95, 93	89 ± 9.3 (10.4)
	G30033	ditto	12	119, 74, 80, 118, 87, 83, 66, 91, 80, 75, 80, 120	89 ± 19.1 (21.4)
	G28279	ditto	12	110, 103, 77, 85, 115, 109, 87, 109, 70, 79, 75, 95	93 ± 15.6(16.9)
	G28273	ditto	12	95, 96, 85, 94, 92, 98, 91, 113, 88, 96, 95, 113	96 ± 8.6 (8.9)
	G34048	ditto	6	86, 105, 94, 96, 81, 65	88 ± 14.1 (16.1)
	GS17794	ditto	8	85, 71, 116, 107, 102, 94, 85, 90	94 ±14.2 (15.1)
Molasses	Atrazine	ditto	0		
	G30033	ditto	0		
	G28279	ditto	0		
	G28273	ditto	0		
	G34048	ditto	4	81, 72, 70, 80	76 ± 5.5 (7.2)
	GS17794	ditto	2	109, 118	113
Sugar	Atrazine	ditto	0		
	G30033	ditto	0		
	G28279	ditto	0		
	G28273	ditto	0		
	G34048	ditto	4	91, 98, 79, 84,	88 ± 8.5 (9.6)
	GS17794	ditto	2	79, 73	76

TABLE C.2. Summary of Storage Conditions.				
Matrix	Storage Temperature (°C)	Actual Storage Duration (months)	Metabolites	Interval of Demonstrated Storage Stability (months)
Sugarcane RAC	Frozen	Up to 8.4	Chloro-residues except G28273	25
		Up to 8.4	G28273	12
		Up to 34.7	Hydroxy-metabolites	36
Molasses		Up to 8.1	Chloro-residues except G28273	25
		Up to 8.4	G28273	12
		Up to 34.7	Hydroxy-metabolites	36
Sugar		Up to 8.1	Chloro-residues except G28273	25
		Up to 8.4	G28273	12
		Up to 34.7	Hydroxy-metabolites	36

TABLE C.3. Atrazine in Processed Sugarcane Commodities: Residue Results1									
		lbs ai/A	Atrazine	G30033	G-28279	G-28273	G34048	GS17794	Total[1]
Sugarcane	Control	0	<0.05	<0.05	<0.05	<0.05	<0.01	<0.01	
	1X	10	<0.05	<0.05	<0.05	<0.05	<0.01	<0.01	
	3x	30	0.15	<0.05	<0.05	<0.05	<0.01	<0.01	
	5x	50	1.5	<0.05	<0.05	<0.05	<0.01	<0.01	<1.67
Molasses	Control	0	<0.05	0.06	<0.05	<0.05	<0.01	<0.01	
	1x	10	<0.05	0.08	<0.05	<0.05	<0.01	<0.01	
	5x	50	<0.05	0.08	<0.05	<0.05	<0.01	<0.01	<0.25
Sugar	Control	0	<0.05	<0.05	<0.05	<0.05	<0.01	<0.01	
	1x	10	<0.05	<0.05	<0.05	<0.05	<0.01	<0.01	
	5x	50	<0.05	<0.05	<0.05	<0.05	<0.01	<0.01	<0.22

[1] The LOD is 0.05 ppm for atrazine, G30033, G28279, and G28273. It is 0.01 ppm for G34048 and GS17794. The total is the sum of atrazine plus its chloro-metabolites plus its hydroxy- metabolites

Table C.4. Summarized Residue Results for Atrazine in Processed Sugarcane Commodities – Parent only and Parent plus Chloro-Metabolites only					
RAC	Processed Commodity	Total Rate (lb ai/A) [1]	PHI (days)	Combined chloro-Residues at 5x (Atrazine per se at 5X)(ppm)	Processing Factor
Sugarcane	RAC	50	30	<1.65 (1.5)	NA
	Molasses			<0.20 (<0.05)	0.12 (0.033)
	Sugar			<0.20 (<0.05)	0.12 (0.033)

[1] The proposed maximum seasonal use rate is 10 lb ai/A for sugarcane. The highest use rate in the current field trial was a 5x rate.

[2] The LOQ is 0.05 ppm for each chloro-metabolite and 0.20 ppm for the combined chloro-metabolites.

3 Taking the value of 0.08 ppm for G30033 to be equivalent to <0.005 since the control is 0.06 ppm.

4 The chloro-metabolites are Atrazine, G30033, G28279 and 28273. G34048 and GS17794 are hydroxyl-metabolites.

D. CONCLUSION

This sugarcane processing study is adequate to show that residues of atrazine, per se, are not concentrated, but are reduced when sugarcane is processed into molasses or sugar. Residues of atrazine were found at 1.5 ppm in the RAC, but were <0.05 ppm in sugar and molasses. No residues of any of the other metabolites were found in raw sugarcane, or molasses, or refined sugar. Parent atrazine is expected to be by far the most predominant residue in sugarcane.

E. REFERENCES

DP Number: 272006
Subject: Atrazine. HED Product and residue Chemistry Chapter
From: C. Eiden and D. Soderberg
To: Kimberly Lowe
Dated: 16 April 2002

F. DOCUMENT TRACKING

RDI: David Soderberg (30 Aug 2007); William Donovan (30 Aug 2007); Cathy Eiden (30 Aug 2007).
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